At page 121, line 12, please delete "C (asp)" all three occurrences and substitute therefor --C (ala)--.

At page 122, line 11, please delete "C (asp)" all three occurrences and substitute therefor --C (ala)--.

IN THE CLAIMS:

Please cancel claims 1-62 and add new claims 63-147 as follows consistent with the restriction requirement mailed on December 10, 1997 in the above identified parent application, without prejudice.

Please add new claims 63-147 as follows:

--63. An isolated infectious recombinant respiratory syncytial virus (RSV) comprising a RSV genome or antigenome, a major nucleocapsid (N) protein, a nucleocapsid phosphoprotein (P), a large polymerase protein (L), and a RNA polymerase elongation factor, wherein a modification is introduced within the genome or antigenome comprising a deletion, insertion, substitution, rearrangement, or nucleotide modification of a cis-acting regulatory sequence within the recombinant RSV genome or antigenome.

64. The recombinant RSV of claim 63, wherein the cis-acting regulatory sequence is a gene-start (GS) signal or a (GE) signal.

65. The recombinant RSV of claim 64, wherein a GS or GE signal is deleted or inserted in the genome or antigenome.

66. The recombinant RSV of claim 64, wherein a GS or GE signal is substituted in the genome or antigenome by a heterologous GS or GE sequence.

67. The recombinant RSV of claim 66, wherein the heterologous GS or GE sequence is of a different RSV gene.

68. The recombinant RSV of claim 67, wherein a GE signal of the RSV NS1 or NS2 gene is replaced by a corresponding GE sequence of the RSV N gene.

69. The recombinant RSV of claim 66, wherein the heterologous GS or GE sequence is of a heterologous negative stranded virus.

70. The recombinant RSV of claim 69, wherein the heterologous GS or GE sequence is of a human RSV A or RSV B subgroup.

71. The recombinant RSV of claim 69, wherein the heterologous GS or GE sequence is of a non-human RSV.

72. The recombinant RSV of claim 70, wherein the heterologous GS or GE sequence is of a bovine RSV.

73. The recombinant RSV of claim 70, wherein the heterologous GS or GE sequence is of a parainfluenza virus (PIV).

74. The recombinant RSV of claim 73, wherein the heterologous GS or GE sequence is of a PIV3 virus.

75. The recombinant RSV of claim 64, wherein a nucleotide sequence of a gene-start (GS) or gene-end (GE) signal is altered in the genome or antigenome.

76. The recombinant RSV of claim 64, wherein a gene-start (GS) or gene-end (GE) signal is rearranged by changing a position of the (GS) or gene-end (GE) signal in the recombinant genome or antigenome.

77. The recombinant RSV of claim 63, wherein the cis-acting regulatory sequence occurs within a 3' leader, 5' trailer or intergenic region of the RSV genome or antigenome.

78. The recombinant RSV of claim 77, wherein the cis-acting regulatory sequence is a RSV promoter element.

.79. The recombinant RSV of claim 78, wherein a promoter element is deleted or inserted in the genome or antigenome.

80. The recombinant RSV of claim 78, wherein a promoter element is substituted in the genome or antigenome by a heterologous promoter element.

81. The recombinant RSV of claim 80, wherein the heterologous promoter element is of a different RSV gene.

82. The recombinant RSV of claim 80, wherein the heterologous promoter element is of a heterologous negative stranded virus.

83. The recombinant RSV of claim 82, wherein the heterologous promoter element is of a human RSV A or RSV B subgroup.

84. The recombinant RSV of claim 82, wherein the heterologous promoter element is of a non-human RSV.

85. The recombinant RSV of claim 84, wherein the heterologous GS or GE sequence is of a bovine RSV.

86. The recombinant RSV of claim 82, wherein the heterologous promoter element is of a parainfluenza virus (PIV).

87. The recombinant RSV of claim 86, wherein the heterologous promoter element is of a PIV3 virus.

88. The recombinant RSV of claim 78, wherein a nucleotide sequence of a promoter element is altered in the genome or antigenome.

89. The recombinant RSV of claim 78, wherein a promoter element is rearranged by changing a position of the promoter element in the recombinant genome or antigenome.

90. The recombinant RSV of claim 63, wherein a further modification is introduced within the recombinant genome or antigenome comprising a partial or complete gene deletion, a change in gene position, or one or more nucleotide change(s) that modulate expression of a selected gene.

91. The recombinant RSV of claim 90, wherein a RSV gene is deleted in whole or in part.

92. The recombinant RSV of claim 91, wherein a SH, NS1, NS2, or G gene is deleted in whole or in part.

93. The recombinant RSV of claim 90, wherein expression of a selected RSV gene is reduced or ablated by introduction of one or more translation termination codons.

94. The recombinant RSV of claim 90, wherein expression of a selected RSV gene is reduced or ablated by introduction of multiple translation termination codons.

95. The recombinant RSV of claim 90, wherein expression of a selected RSV gene is reduced or ablated by introduction of a frame shift mutation in the gene.

96. The recombinant RSV of claim 90, wherein expression of a selected RSV gene is modulated by introduction, modification or ablation of a translational start site within the gene.

97. The recombinant RSV of claim 90, wherein a position of one or more gene(s) in the recombinant genome or antigenome is altered relative to a RSV promoter.

98. The recombinant RSV of claim 97, wherein said position of said one or more gene(s) is changed to a more promoter-proximal or promoter-distal location by deletion or insertion of a coding or non-coding polynucleotide sequence within the recombinant genome or antigenome upstream of said one or more gene(s).

99. The recombinant RSV of claim 97, wherein positions of multiple genes in the recombinant genome or antigenome are altered by changing their relative gene order.

100. The recombinant RSV of claim 63, wherein the recombinant genome or antigenome is further modified to incorporate one or more attenuating mutation(s) present in one or more biologically derived mutant human RSV strain(s).

101. The recombinant RSV of claim 100, wherein the recombinant genome or antigenome is further modified to incorporate at least one and up to a full complement of attenuating mutations present within a panel of biologically derived mutant human RSV strains, said panel comprising cpts RSV 248 9ATCC VR 2450), cpts RSV 248/404 (ATCC VR 2454), cpts RSV 248/955 (ATCC VR 2453), cpts RSV 530 (ATCC VR 2452), cpts RSV 530/1009 (ATCC VR 2451), cpts RSV 530/1030 (ATCC VR 2455), RSV B-1 cp52/2B5 (ATCC VR 2542), and RSV B-1 cp-23 (ATCC VR 2579).

102. The recombinant RSV of claim 100, wherein the recombinant genome or antigenome is further modified to incorporate at least one and up to a full complement of attenuating mutations specifying an amino acid substitution at Val267 in the RSV N gene, Glu218 and/or Thr523 in the RSV F gene, Cys319 Phe 521, Gln831, Met1169, Tyr1321 and/or His 1690 in the RSV polymerase gene L, and a nucleotide substitution in the gene-start sequence of gene M2.

103. The recombinant RSV of claim 100, wherein the recombinant genome or antigenome incorporates at least two attenuating mutations.

104. The recombinant RSV of claim 63, wherein the recombinant genome or antigenome comprises a partial or complete human RSV genome or antigenome of one RSV subgroup or strain combined with a heterologous gene or gene segment from a different, human or non-human RSV subgroup or strain to form a chimeric genome or antigenome.

105. The recombinant RSV of claim 104, wherein the heterologous gene or gene segment is from a human RSV subgroup A, human RSV subgroup B, bovine RSV, or murine RSV.

106. The recombinant RSV of claim 104, wherein the chimeric genome or antigenome comprises a partial or complete human RSV A subgroup genome or antigenome

combined with a heterologous gene or gene segment encoding a RSV F, G or SH glycoprotein or a cytoplasmic domain, transmembrane domain, ectodomain or immunogenic epitope thereof from a human RSV B subgroup virus.

107. The chimeric RSV of claim 106, wherein both human RSV B subgroup glycoprotein genes F and G are substituted to replace counterpart F and G glycoprotein genes in a partial RSV A genome or antigenome.

108. The recombinant RSV of claim 106, wherein the chimeric genome or antigenome comprises a partial or complete human RSV B subgroup genome or antigenome combined with a heterologous gene or gene segment from a human RSV A subgroup virus.

109. The recombinant RSV of claim 104, wherein the chimeric genome or antigenome comprises a partial or complete RSV background genome or antigenome of a human or bovine RSV combined with a heterologous gene or genome segment of a different RSV to form a human-bovine chimeric RSV genome or antigenome.

110. The recombinant RSV of claim 63, wherein the recombinant genome or antigenome incorporates a heterologous gene or genome segment from parainfluenza virus (PIV).

111. The recombinant RSV of claim 110, wherein the gene or genome segment encodes a PIV HN or F glycoprotein or immunogenic domain or epitope thereof.

112. The recombinant RSV of claim 110, wherein the genome segment encodes one or more immunogenic protein(s), protein domain(s) or epitope(s) HPIV1, HPIV2, and/or HPIV3.

113. The recombinant RSV of claim 63, wherein the recombinant genome or antigenome is further modified to encode a non-RSV molecule selected from a cytokine, a T-helper epitope, or a protein of a microbial pathogen capable of eliciting a protective immune response in a mammalian host.

114. The recombinant RSV of claim 63 which is a virus.

115. The recombinant RSV of claim 63 which is a subviral particle.

116. The recombinant RSV of claim 63, formulated in a dose of 103 to 106 PFU of attenuated virus.

117. A method for stimulating the immune system of an individual to induce protection against respiratory syncytial virus, which comprises administering to the individual an immunologically sufficient amount of the isolated attenuated recombinant RSV of claim 1.

118. The method of claim 117, wherein the recombinant virus is administered in a dose of 103 to 106 PFU of the attenuated RSV.

119. The method of claim 117, wherein the recombinant virus is administered to the upper respiratory tract.

120. The method of claim 119, wherein the recombinant virus is administered by spray, droplet or aerosol.

121. The method of claim 117, wherein the recombinant virus is administered to an individual seronegative for antibodies to RSV or possessing transplacentally acquired maternal antibodies to RSV.

122. A vaccine to induce protection against RSV, which comprises an immunologically sufficient amount of the isolated attenuated recombinant RSV of claim 1 in a physiologically acceptable carrier.

123. The vaccine of claim 122, formulated in a dose of 103 to 106 PFU of the attenuated RSV.

124. The vaccine of claim 122, formulated for administration to the upper respiratory tract by spray, droplet or aerosol.

125. The vaccine of claim 122, wherein the recombinant RSV elicits an immune response against human RSV A, human RSV B, or both.

126. An expression vector comprising an isolated polynucleotide molecule encoding a respiratory syncytial virus (RSV) genome or antigenome modified by a deletion, insertion, substitution, rearrangement, or nucleotide modification of a cis-acting regulatory sequence.

127. An isolated polynucleotide molecule comprising a respiratory syncytial virus (RSV) genome or antigenome which is modified by a deletion, insertion, substitution, rearrangement, or nucleotide modification of a cis-acting regulatory sequence.

128. The isolated polynucleotide molecule of claim 127, wherein the cis-acting regulatory sequence is a gene-start (GS) signal or a (GE) signal.

129. The isolated polynucleotide molecule of claim 127, wherein the cis-acting regulatory sequence occurs within a 3' leader, 5' trailer or intergenic region of the RSV genome or antigenome.

130. The isolated polynucleotide molecule of claim 127, wherein the cis-acting regulatory sequence is a RSV promoter element.

131. The isolated polynucleotide molecule of claim 127, wherein a further modification is introduced within the recombinant genome or antigenome comprising a partial or complete gene deletion, a change in gene position, or one or more nucleotide change(s) that modulate expression of a selected gene.

132. The isolated polynucleotide molecule of claim 131, wherein a RSV gene is deleted in whole or in part.

133. The isolated polynucleotide molecule of claim 127, wherein expression of a selected RSV gene is reduced or ablated by introduction of one or more translation termination codons in the recombinant genome or antigenome.

134. The isolated polynucleotide molecule of claim 127, wherein expression of a selected RSV gene is reduced or ablated by introduction of a frame shift mutation in the gene.

135. The isolated polynucleotide molecule of claim 127, wherein expression of a selected RSV gene is modulated by introduction, modification or ablation of a translational start site within the gene.

136. The isolated polynucleotide molecule of claim 127, wherein a position of one or more gene(s) in the recombinant genome or antigenome is altered relative to a RSV promoter.

137. The isolated polynucleotide molecule of claim 127, wherein the recombinant genome or antigenome is further modified to incorporate one or more attenuating mutation(s) present in one or more biologically derived mutant human RSV strain(s).

138. The isolated polynucleotide molecule of claim 137, wherein the recombinant genome or antigenome is further modified to incorporate at least one and up to a full complement of attenuating mutations specifying an amino acid substitution at Val267 in the RSV N gene, Glu218 and/or Thr523 in the RSV F gene, Cys319 Phe 521, Gln831, Met1169, Tyr1321 and/or His 1690 in the RSV polymerase gene L, and a nucleotide substitution in the gene-start sequence of gene M2.

139. The isolated polynucleotide molecule of claim 27, wherein the recombinant genome or antigenome comprises a partial or complete human RSV genome or antigenome of one RSV subgroup or strain combined with a heterologous gene or gene segment from a different, human or non-human RSV subgroup or strain to form a chimeric genome or antigenome.

140. The isolated polynucleotide molecule of claim 139, wherein the heterologous gene or gene segment is from a human RSV subgroup A, human RSV subgroup B, bovine RSV, or murine RSV.

141. The isolated polynucleotide molecule of claim 140, wherein the chimeric genome or antigenome comprises a partial or complete human RSV A subgroup genome or antigenome combined with a heterologous gene or gene segment encoding a RSV

F, G or SH glycoprotein or a cytoplasmic domain, transmembrane domain, ectodomain or immunogenic epitope thereof from a human RSV B subgroup virus.

142. The isolated polynucleotide molecule of claim 141, wherein both human RSV B subgroup glycoprotein genes F and G are substituted to replace counterpart F and G glycoprotein genes in a partial RSV A genome or antigenome.

143. The recombinant RSV of claim 127, wherein the recombinant genome or antigenome comprises a partial or complete RSV background genome or antigenome of a human or bovine RSV combined with a heterologous gene or genome segment of a different RSV to form a human-bovine chimeric RSV genome or antigenome.

144. The isolated polynucleotide molecule of claim 127, wherein the recombinant genome or antigenome incorporates a heterologous gene or genome segment from parainfluenza virus (PIV).

145. The isolated polynucleotide molecule of claim 27, wherein the recombinant genome or antigenome is further modified to encode a non-RSV molecule selected from a cytokine, a T-helper epitope, or a protein of a microbial pathogen capable of eliciting a protective immune response in a mammalian host.

146. A method for producing an infectious respiratory syncytial virus (RSV) particle from one or more isolated polynucleotide molecules encoding said RSV, comprising:

expressing in a cell or cell-free lysate an expression vector comprising an isolated polynucleotide comprising a recombinant RSV genome or antigenome which is modified by a deletion, insertion, substitution, rearrangement, or nucleotide modification of a cis-acting regulatory sequence.

147. The method of claim 146, wherein the recombinant RSV genome or antigenome and the N, P, L and RNA polymerase elongation factor proteins are expressed by two or more different expression vectors.—